PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

FEB 1 0 2006

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NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis.1(c))

To:

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Date of mailing *(day/month/year)* 09 February 2006 (09.02.2006)	
Applicant's or agent's file reference UMD-0067	**IMPORTANT NOTICE**

International application No. PCT/US2004/024351	International filing date *(day/month/year)* 29 July 2004 (29.07.2004)	Priority date *(day/month/year)* 30 July 2003 (30.07.2003)

Applicant UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Philippe Becamel
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 70 90

Form PCT/IB/326 (January 2004)

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference UMD-0067	FOR FURTHER ACTION	See item 4 below
International application No. PCT/US2004/024351	International filing date *(day/month/year)* 29 July 2004 (29.07.2004)	Priority date *(day/month/year)* 30 July 2003 (30.07.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

   ☒ Box No. I   Basis of the report

   ☐ Box No. II   Priority

   ☐ Box No. III   Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

   ☐ Box No. IV   Lack of unity of invention

   ☒ Box No. V   Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   ☐ Box No. VI   Certain documents cited

   ☐ Box No. VII   Certain defects in the international application

   ☒ Box No. VIII Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 30 January 2006 (30.01.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer **Philippe Becamel**
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

<table>
<tr>
<td>To:
JANE MASSEY LICATA
LICATA & TYRRELL P.C.
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MARLTON, NJ 08053</td>
<td>PCT REC'D 1 8 MAR 2005
WIPO   PCT</td>
</tr>
</table>

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REC'D 1 8 MAR 2005

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

<table>
<tr>
<td>Applicant' s or agent's file reference

UMD-0067</td>
<td>Date of mailing <i>(day/month/year)</i>   16 MAR 2005
FOR FURTHER ACTION
See paragraph 2 below</td>
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PCT/US04/24351</td>
<td>International filing date <i>(day/month/year)</i>

29 July 2004 (29.07.2004)</td>
<td>Priority date <i>(day/month/year)</i>

30 July 2003 (30.07.2003)</td>
</tr>
</table>

International Patent Classification (IPC) or both national classification and IPC

IPC(7): G01N 33/48 and US Cl.: 702/19

Applicant

UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY

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1. This opinion contains indications relating to the following items:

☒ Box No. I   Basis of the opinion

☐ Box No. II   Priority

☐ Box No. III   Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

☐ Box No. IV   Lack of unity of invention

☒ Box No. V   Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

☐ Box No. VI   Certain documents cited

☐ Box No. VII   Certain defects in the international application

☒ Box No. VIII   Certain observations on the international application
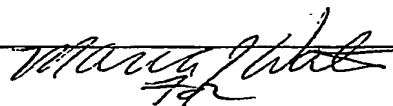
2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis(b)* that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

<table>
<tr>
<td>Name and mailing address of the ISA/ US
    Mail Stop PCT, Attn: ISA/US
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<td>Authorized officer

Carolyn Smith

Telephone No. 571-272-1600</td>
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</table>

Form PCT/ISA/237 (cover sheet) (January 2004)

Box No. I   Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing

   ☐ contained in international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2, 4, 6, 8	YES
	Claims	1, 3, 5, 7	NO
Inventive step (IS)	Claims	NONE	YES
	Claims	1-8	NO
Industrial applicability (IA)	Claims	1-8	YES
	Claims	NONE	NO

2. Citations and explanations:

Please See Continuation Sheet

Box No. VIII	Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 3-8 are objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claims indefinite for the following reason(s):

Claims 3, 5, and 7 recite the phrase " according to" which is unclear. It is unclear what parameters and to what degree these parameters must be met to be considered " according to". Claims 4, 6, and 8 are also objected to due to their dependency from the objected claims.

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1, 3, 5, and 7 lack novelty under PCT Article 33(2) as being anticipated by Hytopoulos et al. (US 2002/0169560 A1).

    Hytopoulos et al. disclose a methods and a system using expression data arrays and cluster arrays wherein the expression values have been normalized, filtered, and imputed (abstract and paragraphs 0052 and 0123). The normalization of data represents normal distributions or Gaussian distributions or models. Hytopoulos et al. disclose allowing the user to select K-nearest neighbor imputation mechanism or other data imputation mechanisms (paragraph 0125). Hytopoulos et al. disclose analysis of gene expression data to form clusters (abstract). Hytopoulos et al. disclose identifying genes represented in respective rows (paragraph 0038) which represents a partitioning of rows of microarray data. Hytopoulos et al. disclose mapping rows of expression data (paragraph 0131). Hytopoulos et al. disclose using a computer readable medium in association with a computer including a processor and memory and computer instructions which are configured to cause a computer to process data (claim 15) which represents an algorithm and computer software program and product.

Claims 1-8 lack novelty and inventive step under PCT Article 33(2)-(3) as being motivated by Hytopoulos et al. (US2002/0169560 A1) in view of Cereghini et al. (US 6,496,834 B1).

    Hytopoulos et al. describe a methods and a system using expression data arrays and cluster arrays wherein the expression values have been normalized, filtered, and imputed (abstract and paragraphs 0052 and 0123). The normalization of data represents normal distributions or Gaussian distributions or models. Hytopoulos et al. describe allowing the user to select K-nearest neighbor imputation mechanism or other data imputation mechanisms (paragraph 0125). Hytopoulos et al. describe analysis of gene expression data to form clusters (abstract). Hytopoulos et al. describe identifying genes represented in respective rows (paragraph 0038) which represents a partitioning of rows of microarray data. Hytopoulos et al. describe mapping rows of expression data (paragraph 0131). Hytopoulos et al. describe using a computer readable medium in association with a computer including a processor and memory and computer instructions which are configured to cause a computer to process data (claim 15) which represents an algorithm and computer software program and product. Hytopoulos et al. do not describe repeating a classification expectation-maximization algorithm until the K partitions converge.

    Cereghini et al. describe a method of performing cluster analysis using Gaussian mixture parameters and implementing an Expectation-Maximization clustering algorithm iteratively (abstract). Cereghini et al. describe grouping a set of data into k clusters with k rows (partitioned) (col. 2, lines 57-63). Cereghini et al. describe the expectation-maximization algorithm converges quickly and performing iterations (col. 9, lines 34-42).

    Hytopoulos et al. state that effective mechanisms for analyzing DNA array data are needed to determine which genes or combination of genes are correlated to various human conditions (paragraph 0009). Cereghini et al. state the EM algorithm is robust for noisy data and missing information (col. 7, lines 5-6). Cereghini et al. state cluster analysis does not typically work well with large databases due to memory limitations and the execution times required (col. 2, lines 32-39). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use effective means for analyzing DNA array data, as stated by Hytopoulos et al., by using algorithms supporting large databases, as stated by Cereghini et al. The person of ordinary skill in the art would have been motivated to make that modification in order to find effective ways (as stated by Hytopoulos et al. and Cereghini et al.) of correlating genes to human conditions (as stated by Hytopoulos et al.) by allowing non-statisticians to benefit from advanced

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/24351

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

mathematical techniques available in a relational environment, as stated by Cereghini et al. (col. 2, lines 40-43). Thus, Hytopoulos et al., in view of Cereghini et al. motivate the instant invention.

Claims 1-8 meet the criteria set out in PCT Article 33(4), and thus meet the requirements for industrial applicability because the subject matter claimed can be made or used in industry.